[4110-03]

SUBCHAPTER H—MEDICAL DEVICES

[Docket No. 77N-0255]

MEDICAL DEVICE LISTING

Final Rule

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document sets forth the procedures for the listing of medical devices under the Medical Devices Amendments of 1976. The rule establishes who must list devices, the times for listing, how devices must be listed, and other necessary procedural requirements.

EFFECTIVE DATE: October 10, 1978.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION: The proposal upon which this final regulation is based was published in the FEDERAL REGISTER of September 30, 1977 (42 FR 52808), with corrections published October 7, 1977 (42 FR 54574), November 1, 1977 (42 FR 57137), and December 2, 1977 (42 FR 61287). Interested persons were given until November 29, 1977 to comment.

Eighteen comments were received on the proposal. The issues most often raised concerned the definition of a restricted device, the clarification of various other definitions, the requirements for maintenance of the historical file, and the requirement for semiannual updating.

The final regulation is being adopted substantially as proposed, although several changes have been made in response to the comments and to clarify the language of the regulation.

DEFINITIONS

1. Five comments objected to the definition of the term "restricted device" in proposed § 807.3(l) (21 CFR 807.3(l)). These comments stated that the Commissioner of Food and Drugs must designate restricted devices by regulations promulgated under section 520(e) of the act (21 U.S.C. 360j(e)) and could not, except by such regulations, designate all prescription devices under § 801.109 (21 CFR 801.109) as restricted devices.

The Commissioner maintains that the devices that were prescription devices under § 801.109 became restricted devices under section 520(e) of the act by operation of law on the date of enactment of the Medical Device Amendments of 1976.

The issue, however, has been under litigation. In three related cases, *Becton, Dickinson and Company* v. *Food and Drug Administration; United States* v. *Becton, Dickinson and Company*, and *In the Matter of Establishment Inspection of Bard-Parker Division of Becton, Dickinson and Company*, the U.S. District Court for the Northern District of New York ruled that FDA must issue regulations classifying devices as "restricted devices." 448 F. Supp. 776 (N.D. N.Y. 1978), appeal docketed, No. 78-6109 (2d Cir. June 5, 1978). The government is appealing that decision to the U.S. Court of Appeals for the Second Circuit.

Subsequent to the *Becton* decision, two other U.S. District Courts have ruled on the prescription/restricted device issue. In both cases, the courts declined to follow the *Becton* decision.

The U.S. District Court of the Central District of California sustained FDA's position that heart pacemakers, which previously were prescription devices, are now "restricted devices," and granted FDA access to related records. *In the Matter of the Establishment Inspection of American Technology, Inc.*, No. CV 78-1727-LEW (C.D. Cal., filed June 14, 1978).

The U.S. District Court for the District of Massachusetts granted a motion to quash an administrative warrant sought by FDA for records relating to endotracheal tubes on the basis that the warrant was too general. On the restricted device issue the Court held:

> I find, however, the device in question is a "restricted device" by reason of having been limited to use by prescription only prior to the enactment of 21 U.S.C. 360j [and] is covered by 21 CFR 801.109. I decline to follow *Becton, Dickinson* v. *FDA*, 448 F. Supp. 776 (N.D. N.Y., 1978).

In Re: Administrative Warrant Issued to the Food and Drug Administration on July 27, 1978 Regarding Portex, Inc. (D. Mass., filed July 28, 1978). The issue is pending also in two related cases before the U.S. District Court for the Western District of Missouri. *United States* v. *Sherwood Medical Industries, Inc., et al.* (No. 77-0890-CV-W-Z) and *In the Matter of Establishment Inspection of Sherwood Medical Industries, Inc.* (No. 77-0265-CV-W-Z). The definition of "restricted device" in § 807.3(l) is consistent with the Commissioner's position in those proceedings.

2. Two comments suggested the definitions of "representative sampling of advertisements" and "representative sampling of any other labeling" in proposed § 807.3 (k) and (l), respectively, need clarification because the phrase, "gives a balanced picture of," is confusing. One comment suggested that these definitions are unnecessary and that the Commissioner should be required to specify the nature of the advertisement and labeling material whenever the agency makes a specific request for labeling and advertisements.

The Commissioner agrees that the definitions need clarification. Therefore, the phrase, "a balanced picture of," has been deleted from § 807.3 (k) and (l) in the final regulation. However, the Commissioner rejects the suggestion that these definitions are unnecessary because they are needed to explain terms used in § 807.31(e) (2) and (3) of the final regulation (21 CFR 807.31(e) (2) and (3)). Section 510(j)(1) of the act (21 U.S.C. 360(j)(1)) requires only that a "representative sampling" of advertisements and labeling be submitted with device lists (Form FD-2892). Therefore, the Commissioner is not required to specify the nature of the advertisements and labeling to be submitted. Section 807.31, which allows owners or operators to maintain the advertisements and labeling in a historical file for their convenience, does not impose any additional legal requirements on the Commissioner to specify the nature of the advertisements and labeling. However, FDA requests for representative sampling of advertisements or any other labeling will, to the extent possible, specify the nature and the basis for the request to further aid the owner or operator in submitting advertisements and labeling.

3. One comment asked why labels and package inserts were excluded from the definition of "representative sampling of any other labeling" in proposed § 807.3(l). Another comment questioned how the labeling for an electronic instrument, which consists of nameplates, technical manuals (or instruction sheets), specification sheets, and advertisements relates to the terms "label," "package insert," and "any other labeling."

The Commissioner realizes that both the terms "label" and "package insert" are included within the term "labeling," as defined in section 201(m) of the act (21 U.S.C. 321(m)). Nevertheless, section 510(j)(1)(B)(ii) of the act provides that "the label and package insert * * * and a representative sampling of any other labeling" are required (see § 807.31(e)(3)). Thus, "any other labeling" includes written, printed, or graphic matter (other than the label or package insert) (1) upon any article or any of its containers and wrappers or (2) accompanying such article (e.g., specification sheets, maintenance manuals, technical manuals which do not give instructions for the use of the device, and catalogs).

In reference to the comment concerning electronic devices, the Commissioner notes that the definitions of "label" and "labeling" in section 201 (k) and (m) of the act, respectively, are controlling. To simplify greatly, a "label" is written information on, or attached to, a device; a "package insert" is any labeling accompanying the device that gives instructions for its use. ("Labeling" is a broad term encompassing both "label" and "package insert.") Therefore, for electronic devices, nameplates would be considered labels; technical manuals that include instructions for use or instruction sheets that accompany the device would be considered package inserts; and specification sheets would be "any other labeling"—other than labels or package inserts. Advertisements would not be "labeling" unless they accompany the device.

4. A new definition has been added to the final regulation. The term "material change" has been added to § 807.3 as paragraph (m) to clarify revised § 807.31(b). This is discussed further under the comments relating to proposed § 807.31.

WHO MUST LIST

5. One comment proposed that X-ray manufacturers be exempted from listing X-ray equipment and parts with the Bureau of Medical Devices because they are listed with the Bureau of Radiological Health.

The Commissioner rejects this proposal. Part 1002 of Title 21 of the Code of Federal Regulations (21 CFR Part 1002), governing records and reports issued under the authority of section 360A of the Public Health Service Act (42 U.S.C. 263i), provides for initial and annual reports to the Bureau of Radiological Health. However, the reports only provide information on operational characteristics of electronic products relating to radiation emission. The authority in section 510 of the act is much broader. It authorizes the Commissioner to require the submission of labeling (as set forth in § 807.31(a) and (b)) not merely information relating to electronic product radiation safety. In addition, firms must supply other information on Form FD-2892, e.g., classification name and number. Because the regulations issued under section 360A of the Public Health Service Act do not provide for the submission of information required by these regulations, the Commissioner concludes that owners or operators of firms producing equipment regulated by both the Bureaus of Radiological Health and Medical Devices must complete Form FD-2892 in its entirety. To eliminate duplication of requirements, the Bureau of Medical Devices will review initial and annual reports submitted to the Bureau of Radiological Health under part 1002 before contacting owners or operators for labeling and advertisements.

6. Section 807.20(a) (21 CFR 807.20(a)) provides that listing information may be submitted by the parent, subsidiary, or affiliate company for all the establishments under the control of one of these organizations when operations are conducted at more than one establishment and there exists joint ownership and control among all the establishments.

One comment suggested that this section be modified to provide that the listing information may be submitted by the parent, subsidiary, or affiliated company for all establishments "including foreign facilities."

The Commissioner concurs with the comment and has revised § 807.20(a) of the final regulation to include reference to foreign establishments. Section 807.40(b) has also been changed to permit a parent, subsidiary, or affiliate company of a foreign establishment to list and maintain the historical file on behalf of the foreign establishment.

7. One comment requested clarification as to whether registration and listing are required only for firms engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of "finished" devices. Also, the comment suggested that firms manufacturing or selling components of in vitro diagnostic products for use in systems manufactured by other firms, if required to register and list, should be required to submit labeling to the Food and Drug Administration for review to protect the public from exposure to products not in compliance with current in vitro diagnostic labeling regulations.

The Commissioner believes that § 807.20(a) as revised in this final regulation adequately specifies who must register and list. Under § 807.20(a), some owners or operators, in addition to those engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of "finished" devices, are required to list, e.g., owners or operators that (1) repackage or relabel a device, (2) manufacture components or accessories that are ready to be used for any intended health related purpose and are packaged or labeled for such health related purpose (e.g., blood fillers and hemodialysis tubing), or (3) manufacture devices which of necessity must be further processed by a licensed practitioner or other qualified person to meet the needs of a particular patient (e.g., a manufacturer of ophthalmic lens blanks). An owner or operator should review § 807.65 (21 CFR 807.65), which discusses exemptions from registration for device establishments. Any owner or operator who is exempt from registration is exempt from listing. In addition, any owner or operator is exempt from listing a particular device if the production of that device does not subject the owner or operator to the requirement of registration.

In response to the second comment, the Commissioner believes that § 807.31(e) will enable FDA to secure and to review labeling, when necessary, of firms manufacturing or selling components of in vitro diagnostic devices for use in systems manufactured by other firms. Accordingly, the Commissioner rejects the suggestion that this material be submitted routinely to FDA.

8. Two comments stated that manufacturers of devices that do not enter interstate commerce should be specifically exempted from the provisions of proposed § 807.20(a). These comments stated that the presumption of interstate commerce is rebuttable and that some devices do not enter commerce at all.

These comments raise the question of the applicablity of the regulation in two situations: (1) Where a device is not marketed at all, and (2) where it is manufactured and marketed only intrastate. The Commissioner advises with respect to the first situation that only those devices in commercial distribution (as defined in § 807.3(b)) must be listed. In response to the second issue, the Commissioner does not accept the implication in the comment that section 510 of the act applies only to devices that have been shown to move in interstate commerce. Section 510(b) of the act requires the annual registration of every establishment "in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device * * *." See also section 510(c) and (d) of the act relating to initial and additional registration. Similarly, section 510(h) of the act provides: "Every establishment in any State registered with the [FDA] * * * shall be subject to inspection * * *." Under section 510(j) of the act, of course, any establishment required to register may also be required to submit listing information.

The Commissioner notes that section 510 of the act specifically does not require a showing of movement in interstate commerce. Compare section 301(a) of the act (21 U.S.C. 331(a)) relating to the introduction of adulterated or misbranded devices into interstate commerce. When section 510 was initially enacted in 1962 (Pub. L. 87-781, Title III, § 302), Congress specifically made findings that the registration and inspection of intrastate esablishments were necessary because of their impact on interstate commerce.

See section 301 of Pub. L. 87-781. In enacting the Medical Device Amendments of 1976 (Pub. L. 94-295), Congress further expanded FDA's authority to regulate devices without regard to specific showings of movement in interstate commerce. See section 304(a)(2) of the act (21 U.S.C. 334(a)(2)), authorizing the seizure of any adulterated or misbranded device when and where found with no requirement to establish interstate commerce, and section 709 of the act (21 U.S.C. 379a), establishing a presumption of interstate commerce in other regulatory matters involving devices. Congress expressly stated its intention to expand FDA's intrastate authority over devices in House Report No. 94-853, Medical Device Amendments, February 29, 1976, at page 15.

9. Two comments suggested that the requirement in proposed § 807.20(a) "to submit a list of every device in commercial distribution" be modified to be consistent with the requirement in proposed § 807.22(b) (21 CFR 807.22(b)) that "devices having variations in physical characteristics such as size, package, shape, color, or composition should be considered to be one device, provided the variation does not change the function or intended use of the device." The comments noted that § 807.22(b) does not require the submission of a list including "every" device.

The Commissioner agrees with the comment and has revised § 807.20(a) by eliminating the word "every" and rephrasing the requirement to read: "to submit listing information for those devices in commercial distibution."

10. Section 807.20(a)(2) of the final regulation has been changed to eliminate duplicate listing by exempting an owner or operator who only manufactures devices according to another owner or operator's specifications for commercial distribution by the owner or operator initiating the specifications. As proposed, both parties would have been required to list the same product.

Time for Listing

11. Several comments objected to the imposition of the December 31, 1977 deadline for listing. These comments asserted that there was no requirement to list devices with FDA until FDA issued final device listing regulations.

The Commissioner notes that device listing is required by section 510(j) of the act and is not dependent on the issuance of a final regulation. In the Federal Register of December 28, 1976 (41 FR 56397), FDA gave notice that device listing requirements would be implemented in 1977. Form FD-2892 and the accompanying Device Listing Information and Instructions were sent to Medical Device Establishments in October 1977 to enable device listing by December 31, 1977. However, the Commissioner has determined that the regulation shall not become effective until October 10, 1978. This will allow ample time for submission of forms by owners or operators who did not receive a listing packet in time to list by December 31, 1977, or who did not have sufficient time for other reasons, such as contacting foreign suppliers or affiliates. Section 807.21 has been changed accordingly. The Commissioner believes that the effective date of October 10 1978, will alleviate the need of granting further extensions of time to submit the forms.

12. One comment suggested that the words "or as changes occur" be added to the last sentence of proposed § 807.21, which requires an owner or operator to "update its device listing information every June and December." This change will make § 807.21 consistent with 807.30(b), which requires an owner or operator to update its "device listing information during each June and December or, at its discretion, at the time the change occurs."

The Commissioner agrees with the comment and has changed § 807.21 by adding the phrase "or, at its discretion, at the time the change occurs."

How to Submit Listing

13. Two comments suggested that proposed § 807.25(f) be revised to allow the submission of computer-generated forms in lieu of the listing forms provided by FDA. The comments also suggested that FDA assign blocks of numbers so that registered establishments without access to a computer could preprint their forms with various repetitive information.

The Commissioner observes that proposed § 807.22(b) provides that tapes for computer input may be submitted if equivalent in all elements of information specified in Form FD-2892. The Commissioner would prefer the submission of computer tapes. However, should there be situations where it is not possible for the owner or operator to provide a computer tape compatible with FDA equipment, hard copy computer output would be accepted as equivalent to computer tapes, provided that review and approval is secured from FDA before submission in accordance with § 807.22(b).

Upon request to the Bureau of Medical Devices at the address given in § 807.22(a), FDA will provide blocks of numbers to be used as the document number by owners or operators who prefer to preprint their own listing forms.

14. One comment suggested that proposed § 807.22(c) be modified to indicate that the initial distributor of an imported device may submit device listing information on behalf of a foreign establishment if the initial distributor is: (1) A parent, subsidiary, or affiliate company of the foreign manufacturer where joint ownership and control exist, as provided in proposed § 807.20, or (2) the only domestic distributor of that foreign manufacturer and, in addition, submits to FDA a letter from the foreign establishment authorizing the initial distributor to list and maintain a historical file on the foreign establishment's behalf.

The Commissioner has reviewed the listing requirements for initial distributors and has made the following changes in the final regulation to clarify those requirements. Section 807.22(c) has been changed to require the initial distributor to submit form FD-2892 and to maintain the historical file for those imported devices (1) for which the specifications have been initiated or developed by the initial distributor or (2) which have been repackaged or relabeled by the initial distributor (see § 807.20(a) (1) and (2)). The listing requirements in § 807.22(c)(3) remain unchanged from proposed § 807.22(c) if the initial distributor did not initiate or develop the specifications for the device or repackage or relabel the device.

Section 807.40(b) (21 CFR 807.40(b)) has been changed to allow a parent, subsidiary, or affiliate company of the foreign manufacturer or an initial distributor, who is a sole initial distributor, to list and maintain the historical file for a foreign manufacturer upon meeting the other requirements in the paragraph. The Commissioner notes that the initial distributor may, in turn, distribute the product to multiple domestic distributors and still be authorized to list for the foreign establishment.

Information Required for Device Listing

15. One comment stated that the device listing information and instructions accompanying form FD-2892 contain terms that are not adequately defined and instructions that are unclear and confusing.

The Commissioner believes that the device listing information and instructions accompanying form FD-2892 give adequate directions for submitting listing information for most situations. The agency will provide detailed guidance in those situations where any owner or operator is confused as to the appropriate procedures to follow in listing devices. If many owners or operators need to have these instructions clarified, updated instructions will be provided at a later date.

16. One comment questioned the statutory authority for question 14 on form FD-2892. The question reads, "Is the device, as labeled, intended for distribution to and use by the general public?" The comment expressed concern that this information would be used to classify a device as a "restricted" device.

The Commissioner observes that section 510(j)(1) (A) and (B) (i) and (ii) of the act requires the submission of all labels for each listed device. If FDA required all labels to be submitted with form FD-2892, it could readily be discerned whether the device, as labeled, was intended for distribution to and use by the general public. Question 14 on form FD-2892 allows this information to be provided to FDA without requiring the submission of all labels, which would otherwise burden owners or operators with the additional costs of submitting all labels.

The agency will determine those devices that are restricted devices in accordance with section 520(e) of the act. This determination is not dependent on the answer to question 14. Also, the Commissioner notes that under section 510(j)(1)(D) of the act, FDA may require the submission of the basis for determining that a device is not a restricted device (see § 807.31(e)(5)).

17. One comment objected to the requirement in proposed § 807.25(f)(1) that the device be identified by a common or usual name. The comment stated that identifying a device by a common or usual name would require the addition of that name to the label in order to avoid misbranding under section 502(e)(2) of the act (21 U.S.C. 352(e)(2)). To relieve this problem, it was suggested that the term "common or usual name" on form FD-2892 be changed to "descriptive name."

The Commissioner notes that section 510(j) (1) and (2) (A), (B), and (C) of the act requires that upon initial listing, discontinuance, or a resumption of commercial distribution of a device, its established name, as defined in section 502(e) of the act, must be listed. In section 502(e)(4) of the act,

> * * * the term "established name" with respect to a device means (A) the applicable official name of the device designated pursuant to section 508, (B) if there is no such name and such device is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then any common or usual name of such device.

Because no official names have been established for devices under section 508 of the act and few official names for devices are recognized in an official compendium, the common or usual name must be provided to satisfy the established name requirement of section 510(j) (1) and (2) (A), (B), and (C). The use of a "descriptive name" on form FD-2892 would not comply with the act.

The identification of a common or usual name on form FD-2892 does not change the requirement of section 502(e)(2) of the act that the established name appear on the label to avoid misbranding. However, the Commissioner does not intend to use the designation of the common or usual name on form FD-2892 to enforce section 502(e)(2) of the act because a change in the common or usual name does not require the updating of form FD-2892 (see § 807.30(b)(6) (21 CFR 807.30(b)(6))).

18. One comment suggested that the last phrase of proposed § 807.25(f)(1), which states "* * * that has not been included in any list of devices previously submitted on form FD-2892," be changed to read "* * * distribution that has not been included in any list of devices which have been previously submitted to FDA," because the present wording of the section suggests that more than one device can be included on a form FD-2892. The comment stated that this conflicts with proposed § 807.22(b), which states that "a separate form FD-2892 shall be submitted for each device or device class listed with the Food and Drug Administration."

The Commissioner does not believe that there is any conflict between the provisions of §§ 807.25(f)(1) and 807.22(b). The suggested change to the wording of § 807.25(f)(1) does not significantly change the meaning of that section and therefore is rejected. The Commissioner, however, agrees that only one device can be included on a form FD-2892.

19. One comment suggested that proposed § 807.25(f) (1) through (5) be modified to use the exact wording that appears on form FD-2892, thus permitting the reader of the regulation to know exactly what information has to be supplied even though he does not have a copy of form FD-2892.

The Commissioner agrees that, to the extent possible, all information to be submitted on form FD-2892 should be specified in the regulation. Section 807.25 has been changed accordingly. Section 807.25(f)(1) has been changed to specify that listing information shall state the classification number of the device. Section 807.25(f)(4) has been changed to specify that listing information shall state the establishment type of every domestic or foreign device establishment under joint ownership and control of the owner or operator at which the device is manufactured, repackaged, or relabeled (see paragraph 20 in this preamble). New § 807.25(f)(5) is added to specify that listing information shall state whether the device as labeled is intended for distribution to and use by the general public. New § 807.25(f)(6) has been added to specify that listing information shall state all other general information on form FD-2892. Proposed § 807.25(f)(5) (redesignated § 807.25(f)(7)) has been changed and allows descriptive information other than labeling to describe the intended use of a device when the owner or operator is unable to find an appropriate classification name for the device. A copy of form FD-2892 may be obtained by contacting FDA at the address indicated in § 807.22(a).

20. One comment questioned whether proposed § 807.25(f)(4) should be clarified by adding the words "domestic or foreign" before the words "device establishment."

The Commissioner agrees with the comment and has changed the final regulation accordingly. However, only those establishments under joint ownership and control of the owner or operator must appear on form FD-2892 (see paragraph 19 above).

Updating Device Listing

21. Three comments suggested that the filing of premarket notifications coupled with annual list updating would satisfy the requirement of semiannual list updating and ease the agency's administrative burden.

The Commissioner disagrees with the comment. Section 510(j)(2) of the act requires semiannual updating. In addition, certain information required under listing is not required under premarket notification. Therefore, the filing of premarket notifications coupled with annual list updating will not satisfy the statute. Also, the Commissioner believes that the time involved in submitting updated listing forms is minimal, because, for most devices, a form FD-2892 will be completed only at the time of initial listing.

22. One comment suggested that proposed § 807.30(b)(4), which requires updating device listing whenever there is any material change in any information previously submitted, be modified because the proposed language would require updating any supplemental sheets to form FD-2892, labeling supplied under proposed § 807.25(f)(5), or labeling, advertising, and other information required under proposed § 807.31. The comment indicated that the modification should make this section consistent with proposed § 807.22(b), proposed § 807.30(b) (1) and (2), and the device listing information and instructions accompanying form FD-2892.

Another comment suggested that to eliminate confusion, the word "material" in proposed § 807.30(b)(4) should be changed to "substantial." This com-

ment also suggested that proposed § 807.30 (a) through (c) be modified to use the exact language of form FD-2892.

The Commissioner notes that section 510(j)(2)(D) of the act requires an updated submission for any material change in any listing information submitted under section 510(j)(1), which states what information is required at the time of initial listing, and section 510(j)(2), which states what information is required after initial listing. Proposed § 807.30(b)(4) is consistent with sections 510(j)(2)(D) of the act and does require the updating of supplemental sheets to form FD-2892, labeling supplied under proposed § 807.25(f)(5) (now § 807.25(f)(7) in the final regulation), and labeling, advertisements, and other information required under § 807.31. However, the intent of proposed § 807.30(b)(4) was only to set forth the requirements for updating the listing information on form FD-2892. Therefore, to clarify the requirements for updating form FD-2892, proposed § 807.30 has been changed in its entirety to specify those changes to information required on form FD-2892 which must be updated and the information that must be included for each type of update specified in section 510(j)(2) (A) through (D) of the act.

Revised § 807.30(a) specifies that all changes must be made on form FD-2892. Revised § 807.30(b) reiterates the time when updating is required as indicated in § 807.21. Revised § 807.30(b)(1) specifies the information required when an owner or operator introduces into commercial distribution a device identified with a classification name not currently listed. Revised § 807.30(b)(2) specifies the information required when an owner or operator discontinues commercial distribution of all devices with the same classification name. Revised § 807.30(b)(3) specifies the information required when commercial distribution of a discontinued device is resumed. New § 807.30(b)(4) specifies the information required when a classification name for a previously listed device with multiple classification names has been added or deleted. New § 807.30(b)(5) specifies the information required when changes in block 6, 7, 12, 12a, 13, 13a, 14, 15, 16, or 17 of form FD-2892 occur. New § 807.30(b)(6) indicates which changes to the information required in § 807.25 do not require updating. Proposed § 807.30(c) has been deleted.

Section 807.30, as revised, is consistent with all other sections of the regulation and the information and instructions booklet accompanying form FD-2892 and does not refer to "material" changes.

The suggestion that the exact language of form FD-2892 be used is rejected as being unnecessary. Form FD-2892 and its accompanying device listing information and instructions may be obtained by contacting FDA at the address indicated in § 807.22(a).

23. One comment suggested that proposed § 807.30(b)(2), which requests that the owner or operator give the reason for discontinuing commercial distribution of a device, be deleted. The comment suggests that the reasons for discontinuing commercial distribution might constitute confidential commercial information, and that failure to furnish the reason under the optional terms of the proposed section might give rise to conjecture of a discreditable reason. The owner or operator should not be placed in this conflicting position.

The Commissioner has reevaluated this requirement. In light of the classification name approach to listing, the Commissioner agrees that such information would not be meaningful. The section is revised to delete the request for the reason(s) for discontinuance of commercial distribution.

ADDITIONAL LISTING INFORMATION

24. Two comments requested that a date be specified in § 807.31 from which maintenance of the historical file is required. Six comments stated that a time limit should be set for the retention of labeling and advertisements in the historical file. Some of the suggested time limitations included any reasonable, valid time period established by the manufacturer, 5 years after the labeling or advertisement has been introduced, or 1 year after the device has been discontinued.

The Commissioner concurs with the comments and has revised § 807.31(a) to specify the time from which owners or operators shall maintain labeling and advertisements in the historical file, which is the date of initial listing. Owners or operators shall maintain in the file labeling and advertisements in use on the date of initial listing and in use after October 10, 1978, but before the date of initial listing. Section 807.31(a) has also been changed to specify which labeling and advertisements must be retained in the historical file at the time of initial listing. (This change is discussed in paragraph 25 in this preamble.)

The Commissioner has established a time limit for retention of certain labeling and advertisements for discontinued devices in new § 807.31(c). Generally, the owner or operator may discard labeling and advertisements 5 years after the date of the last shipment of a discontinued device. However, if the device has an anticipated useful life of more than 5 years, the owner or operator must retain, in the historical file until the end of the anticipated useful life of the device, the labeling in use on the date of the last shipment and a representative sampling of all advertisements in use during the 12 months immediately preceding the last shipment of a restricted device. A retention period of 5 years after the last shipment of a discontinued device by an owner or operator was chosen because: (1) Devices can be marketed at the retail level long after discontinuance, (2) labeling and advertisements are used to promote the sale and indicate the use and effectiveness of the device even after it has been discontinued, and (3) commercial distribution of devices is sometimes resumed after discontinuance. A longer period is required for devices with a longer useful life because regulatory problems concerning labeling or advertisements may occur throughout the useful life of the device. The Commissioner has not established a time limit for the retention of labeling and advertisements for devices in commercial distribution because labeling and advertisements are relied upon by users of the device even after they have been discontinued by the manufacturer. If the need for a time limit on the retention of labeling and advertisements of devices in commercial distribution becomes necessary, the Commissioner will establish a time limit that is necessary to protect the public health.

25. One comment stated that section 510(j)(1)(B) (i) and (ii) of the act requires only a record or file of the labels and labeling in use at the time of initial listing. The comment states that to require more than a file of currently used labels and labeling clearly exceeds the scope, intent, and legislative history of section 510(j)(1)(B) (i) and (ii) of the act. Another comment asserted that many changes in labels, labeling, and advertising are typographical or otherwise inconsequential and the requirement to keep all labels, labeling, and advertisements would place an unnecessary burden on the owner or operator in the way of excessive and unproductive recordkeeping. This comment suggested that only significant, substantive changes in labels, labeling, and advertisements be retained

The Commissioner notes that section 510(j)(1) (A) and (B) (i) and (ii) of the act requires only that, upon initial listing, an owner or operator must submit: (1) A copy of all labeling for each unrestricted device subject to sections 514 or 515 of the act (see § 807.31(a)(1)); (2) a copy of all labeling and advertisements for each restricted device (see § 807.31(a) (2)); and (3) a copy of all labels, package inserts, and a representative sampling of any other labeling for each unrestricted

device that is not subject to sections 514 or 515 of the act (see § 807.31(a)(3)). However, section 510(j)(2)(D) of the act requires the submission of any material change in any information previously submitted under section 510(j)(1) (A) and (B) (i) and (ii) of the act. Therefore, the Commissioner rejects the contention that only a record or file of the labeling in use at the time of initial listing may be required. However, the Commissioner agrees that only "material changes" in labeling and advertisements retained under § 807.31(a) must be maintained in the historical file and has added new § 807.31(b) accordingly. (Proposed § 807.31(b) has been changed to § 807.31(e) in the final regulation.)

A definition of the term "material change" has been added in § 807.3(m) to aid owners and operators in complying with § 807.31(b). The Commissioner observes that a material change in the labeling or advertisements for a device may be evidence of a change in the device requiring a premarket notification under § 807.81(a)(3) (21 CFR 807.81(a)(3)).

Also, the Commissioner notes that the definition of "labeling" in section 201(m) of the act includes all "labels" and has shortened the phrase "labels and labeling" to "labeling" in the final regulation.

26. Two comments asserted that the cost of maintaining the historical file will become unjustifiably burdensome on manufacturers of devices in which every lot produced has its own insert with the label values for that lot, e.g., manufacturers of in vitro diagnostic calibrator devices. The comments suggested that labeling for a specific lot of product should only be retained for 6 months beyond the expiration date of the lot or 2 years after the date of initial distribution.

The Commissioner recognizes that, although there are some medical devices in which every lot produced has a unique label value (antisera, reference control sera, and calibration standards) and may be produced to the same specifications, the biological activity or known composition differs with each lot. For proper use, the specific activity or composition must be determined and made available to the user. However, for the purpose of maintaining the historical file, the labeling that contains the actual values is not required. Therefore, the definition of "material change" in § 807.3(m) excludes the labeling containing the actual values for each lot where the biological activity or known composition differs with each lot produced and the product is labeled accordingly. Nevertheless, the owner or operator must retain a copy of the labeling, as required under § 807.31(a), and any labeling to which a material change occurs, as required under § 807.31(b). For example, if value ranges are preprinted and specific values are added for each lot produced, only a copy of that labeling which includes the preprinted value ranges must be maintained.

27. Two comments suggested that proposed § 807.31(a) be modified to allow owners or operators who use separate or central facilities for the reproduction of labels, labeling, and advertisements to have those facilities maintain the historical file for the documents they reproduce. This would eliminate duplication of effort since these facilities retain a copy of all documents they reproduce.

The Commissioner agrees with the comment and has added new § 807.31(d) to allow the contents of the historical file to be maintained in more than one location under certain conditions set forth in that section.

28. One comment suggested that proposed § 807.31(b)(1) be modified to include a definition of "good cause" and to require that the Commissioner accompany any request under that section with an explanation of the reasons for such request.

The Commissioner disagrees with the suggestion to define "good cause" because each request under § 807.31 will be made on a case-by-case basis. However, proposed § 807.31(b)(1), which has been changed to § 807.31(e)(2) in the final regulation, requires that a request for all advertisements will, where feasible, be accompanied by an explanation of the basis for the request.

29. The Commissioner has changed proposed § 807.31(b) to § 807.31(e) in the final regulation and made the following changes in accordance with section 510(j)(1) of the act: New § 807.31(e)(1) requires that, upon request, all labeling for a device subject to sections 514 or 515 of the act shall be submitted to FDA in accordance with section 510(j)(1)(A) of the act. Proposed § 807.31(b)(1) has been changed to § 807.31(e)(2) and is discussed in paragraph 28 above. Proposed § 807.31(b)(2) has been changed to § 807.31(e)(3) and requires that, upon request, labeling for an unrestricted device that is not subject to sections 514 and 515 of the act shall be submitted to FDA in accordance with section 510(j)(1)(B)(ii). Proposed § 807.31(b)(3) has been changed to § 807.31(e)(4). New § 807.31(e)(5) requires that, upon request, a statement of the basis upon which the registrant has determined that the device is not a restricted device shall be submitted to FDA in accordance with section 510(j)(1)(D) of the act. Proposed § 807.31(b) (4) and (5) has been changed to § 807.31(e) (6) and (7), respectively.

NOTIFICATION OF REGISTRANT

30. One comment suggested that the phrase, "does not establish that the holder of the registration is legally qualified to deal in such devices and," be deleted from proposed § 807.35(c). The comment contends that the legal qualifications "to deal in such devices" are not related to these regulations.

The Commissioner disagrees with the comment. Section 807.35(c) states that the assignment of a device listing number does not establish any legal qualifications of the owner or operator to deal in such devices. This statement is correct. The suggested modification may imply by silence that an owner or operator with an assigned device listing number is legally qualified to deal in such devices.

PROCEDURES FOR FOREIGN ESTABLISHMENTS

31. One comment asserted that proposed § 807.40 (b), (c), and (d) should be deleted because: (1) The importer of record must supply the name of the foreign manufacturer of all devices being imported and the request for registration of the foreign manufacturer is merely duplication of paperwork, (2) there are formidable obstacles in requiring rather than requesting foreign manufacturers to list devices, (3) the main focus of FDA's enforcement will rest on the importer, and (4) the importer will bear the legal and financial burden for failure on the part of the foreign manufacturer to complete the listing requirements.

The Commissioner disagrees with the comment. Listing by foreign establishments is required by section 510(i) of the act. Section 807.40(b) has been changed to allow listing on behalf of the foreign establishment by a domestic establishment or the initial distributor as provided in that section. If the foreign establishment does not submit listing information and listing information is not submitted by a domestic establishment or by an authorized initial distributor under § 807.40(b), then the foreign establishment's products will be subject to detention.

32. One comment suggested that proposed § 807.40(b) be modified to limit the requirements on foreign establishments in proposed § 807.25 to only those foreign establishments who are not listed by a parent, subsidiary or affiliate, or an initial distributor.

The Commissioner believes that the revision of § 807.40(b) discussed in paragraph 14 above eliminates this problem. The requirement of § 807.25 remains with the foreign establishment. However, the requirement may be satisfied by a parent, subsidiary or

affiliate, or an initial distributor as provided in § 807.40(b).

33. Two comments suggested that proposed § 807.40(c) should be modified to allow the importation of a device after a premarket notification has been filed rather than after the device is listed. The comments asserted that the premarket notification should be sufficient until the device is required to be listed.

The Commissioner concurs and has changed § 807.40(c) to permit importation before listing. Although the device does not need to be listed before such importation begins, listing must be made at the next interval specified for updating device listing information in § 807.30(b). A premarket notification must be submitted before importation into the United States, if such notice would be required (see § 807.81).

34. One comment suggested modifying proposed § 807.40(c) to allow devices intended solely for investigational use to be imported or offered for import during the period ending on the 90th day after the date of promulgation of regulations prescribing the procedures and conditions required by section 520(g)(2) of the act.

The Commissioner does not believe that the regulation should be changed to reflect this interim period.

NOTE.—Interim final investigational device exemption regulations were published May 12, 1978 (43 FR 20726).

However, until final investigational device exemption regulations are published, a foreign device whose labeling identifies it as an investigational device can be imported without the product first being listed. The device will have to comply with investigational device exemption regulations whenever applicable. The Commissioner notes that investigational device exemption regulations are applicable for intraocular lenses.

GENERAL PURPOSE ARTICLES

35. In the course of implementing the listing procedures, FDA has received several inquiries from manufacturers of in vitro diagnostic products requesting guidance regarding the intent of § 807.65(c) which exempts from registration "a manufacturer of general purpose articles, such as chemical reagents or laboratory equipment whose uses are generally known by persons trained in their use and which are not labeled or promoted for medical uses." Copies of these inquiries are on file with the Hearing Clerk (HFA-305), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857. Many persons were of the opinion that, even though their in vitro diagnostic products were previously exempted from drug registration and listing, they would now be required to register and list these products with FDA since § 807.65(c) included the phrase "not labeled or promoted for medical uses." The persons inquiring believed that promoting the products for use in hospitals, clinical laboratories, etc., would, in itself, be interpreted as promotion for medical use.

In the case of in vitro diagnostic products, general purpose articles are those products that have general laboratory applications but whose uses are not solely in the collection, preparation, and examination of specimens taken from the human body. An in vitro diagnostic product which is a general purpose article must have a use or uses in other areas. Labeling for these products must not make reference to the application of the product in any specific dianostic procedure and must contain only product specifications and, when applicable, meet the labeling requirements of § 809.10(d) (21 CFR 809.10(d)). When appropriate, the labeling may also reference voluntary standards of purity, composition, calibration, etc., developed by organizations such as the American Chemical Society or National Bureau of Standards.

The sale of in vitro diagnostic products that are general purpose articles to clinical laboratories and other medical facilities where there is the probability of diagnostic use does not, in itself, mean that the products are "promoted for medical use." For example, generally a product will not be considered "promoted for medical use" if the labeling contains no reference to diagnostic use and the claims in the labeling do not differ from the claims in the promotional material provided to other types of facilities (i.e., industrial or educational) that also purchase and use the products.

In vitro diagnostic products that meet these requirements are general purpose articles and exempt from registration and listing under § 807.65(c). However, in vitro diagnostic products that are promoted and/or labeled as components or accessories to specific diagnostic systems are not considered general purpose articles. Therefore, they are medical devices subject to registration and listing as required by § 807.20.

ECONOMIC IMPACT

36. One comment stated that an inflation impact statement is necessary. Several other comments expressed concern with the cost of maintaining the historical file.

The Commissioner notes that a copy of the inflation impact assessment is on file with the Hearing Clerk (HFA-305), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857. Section 807.31 of the final regulation provides for limitations on the historical file that should reduce the cost of maintaining the file and allow compliance with section 510(j)(1) of the act. The Commissioner believes that the cost of maintaining the historical file will be less than the cost of requiring the industry to submit labeling and advertisements routinely along with device listing forms. If routine submission of labeling and advertisements were required, most owners or operators would keep a copy of the labeling and advertisements submitted for their own records. Under the historical file system, FDA will require actual submission of such information only when it is necessary to protect the public health.

NATIONAL HEALTH-RELATED ITEMS CODE

37. In the preamble to the proposed listing procedures, FDA announced that support for the National Health Related Items Code (NHRIC) as a system for the identification and numbering of marketed device packages compatible with other numbering systems such as the National Drug Code (NDC) and the Universal Product Code (UPC) would be limited.

The Commissioner observes that no comments were received on this announcement. Therefore, FDA will limit the support of the NHRIC system and no longer maintain the NHRIC data base. Although there is no requirement to place a NHRIC number on device labels, those labelers who wish to use the NHRIC system should contact FDA at the Bureau of Medical Devices, Device Registration and Listing Branch, HFK-124, 8757 Georgia Avenue, Silver Spring, Md. 20910, to obtain a labeler code and other information.

All labelers who participate in the system will be required to develop their own product code and perform any required maintenance to the number system such as adding new codes or deleting old product codes. Those labelers currently participating in the NHRIC system may continue to use the labeler codes assigned but are instructed to no longer submit update information to FDA.

Participants in the NHRIC system should display the NHRIC number prominently in the top third of the principal display panel of the immediate container and of any outside container labeling or wrapper. Owners, operators, and distributors of in vitro diagnostic products previously assigned NDC numbers may retain those numbers, but are required to change the prefix N or NDC to H or HRI as label revisions occur.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 301(p) and (q)(2), 501, 502, 508, 510, 519,

701(a), 52 Stat. 1042-1043 as amended, 1049-1050 as amended, 1055, 76 Stat. 789, 794 as amended, 86 Stat. 562 as amended, 90 Stat. 564-580 (21 U.S.C. 331 (p) and (q)(2), 351, 352, 358, 360, 360l, 371(a)) and under authority delegated to the Commissioner (21 CFR 5.1), Parts 207, 607, and 807 are amended as follows:

PART 207—REGISTRATION OF PRODUCERS OF DRUGS AND LISTING OF DRUGS IN COMMERCIAL DISTRIBUTION

1. In Part 207, by amending § 207.65(i) by adding a sentence at the end of the paragraph, as follows:

§ 207.65 Exemptions for domestic establishments.

* * * * *

(i) * * * This paragraph does not exempt such persons from registration and listing for medical devices required under Part 807 of this chapter.

PART 607—ESTABLISHMENT REGISTRATION AND PRODUCT LISTING FOR MANUFACTURERS OF HUMAN BLOOD AND BLOOD PRODUCTS

2. In Part 607, by amending § 607.65(e) by adding a sentence at the end of the paragraph, as follows:

§ 607.65 Exemptions for blood product establishments.

* * * * *

(e) * * * This paragraph does not exempt such persons from registration and listing for medical devices required under Part 807 of this chapter.

PART 807—ESTABLISHMENT REGISTRATION AND DEVICE LISTING FOR MANUFACTURERS OF DEVICES

3. The heading for Part 807 is revised as set forth above and Part 807 is amended as follows:

a. In Subpart A by amending § 807.3 by adding new paragraphs (i), (j), (k), (l), and (m) to read as follows:

§ 807.3 Definitions.

* * * * *

(i) "Restricted device" means a device for which the Commissioner, by regulation under § 801.109 of this chapter or otherwise under section 520(e) of the act, has restricted sale, distribution, or use only upon the written or oral authorization of a practitioner licensed by law to administer or use the device or upon such other conditions as the Commissioner may prescribe.

(j) "Classification name" means the term used by the Food and Drug Administration and its classification panels to describe a device or class of devices for purposes of classifying devices under section 513 of the act.

(k) "Representative sampling of advertisements" means typical advertising material that gives the promotional claims made for the device.

(l) "Representative sampling of any other labeling" means typical labeling material (excluding labels and package inserts) that gives the promotional claims made for the device.

(m) "Material change" includes any change or modification in the labeling or advertisements that affects the identity or safety and effectiveness of the device. These changes may include, but are not limited to, changes in the common or usual or proprietary name, declared ingredients or components, intended use, contraindications, warnings, or instructions for use. Changes that are not material may include graphic layouts, grammar, or correction of typographical errors which do not change the content of the labeling, changes in lot number, and, for devices where the biological activity or known composition differs with each lot produced, the labeling containing the actual values for each lot.

b. In subpart B by amending § 807.20, by revising the section heading, introductory text of paragraph (a), paragraph (a)(2), and paragraph (b), to read as follows:

§ 807.20 Who must register and submit a device list.

(a) An owner or operator of an establishment not exempt under section 510(g) of the act or subpart D of this part who is engaged in the manufacture, preparation, propagation, compounding, assembly, or processing of a device intended for human use is required to register and to submit listing information for those devices in commercial distribution, except that listing information may be submitted by the parent, subsidiary, or affiliate company for all the domestic or foreign establishments under the control of one of these organizations when operations are conducted at more than one establishment and there exists joint ownership and control among all the establishments. The term "device" includes all in vitro diagnostic products and in vitro diagnostic biological products not subject to licensing under section 351 of the Public Health Service Act. An owner or operator is required to register its name, places of business, and all establishments and to list the devices whether or not the output of the establishments or any particular device so listed enters interstate commerce. The registration and listing requirements shall pertain to any person who:

* * * * *

(2) Manufactures for commercial distribution a device either for itself or for another person. However, a person who only manufactures devices according to another person's specifications, for commercial distribution by the person initiating specifications, is not required to list those devices.

* * * * *

(b) No registration or listing fee is required. Registration or listing does not constitute an admission or agreement or determination that a product is a device within the meaning of section 201(h) of the act.

c. By revising the section heading and text of § 807.21 to read as follows:

§ 807.21 Times for establishment registration and device listing.

An owner or operator of an establishment entering into, or currently engaged in, an operation defined in § 807.3(c) and not currently registered shall register the establishment by October 22, 1977, and submit device listing by October 10, 1978. An owner or operator of an establishment who has not previously entered into an operation defined in § 807.3(c) shall register within 30 days after entering into such an operation and submit device listing information at that time. An owner or operator of an establishment shall update its registration information annually between November 15 and December 31 and shall update its device listing information every June and December or, at its discretion, at the time the change occurs.

d. By revising the section heading and text of § 807.22, to read as follows:

§ 807.22 How and where to register establishments and list devices.

(a) The first registration of a device establishment shall be on form FD-2891 (Initial Registration of Device Establishments). Forms are obtainable on request from the Bureau of Medical Devices (HFK-124), Food and Drug Administration, Department of Health, Education, and Welfare, 8757 Georgia Avenue, Silver Spring, Md. 20910, or from the Food and Drug Administration district offices. Subsequent annual registration shall be accomplished on form FD-2891a (Registration of Device Establishment), which will be furnished by the Food and Drug Administration before November 15 of each year to establish-

ments whose registration for that year was validated under § 807.35(a). The completed form shall be mailed to the above-designated address before December 31 of that year.

(b) The initial listing of devices and subsequent June and December updatings shall be on form FD-2892 (Medical Device Listing). Forms are obtainable upon request as described in paragraph (a) of this section. A separate form FD-2892 shall be submitted for each device or device class listed with the Food and Drug Administration. Devices having variations in physical characteristics such as size, package, shape, color, or composition should be considered to be one device: *Provided,* The variation does not change the function or intended use of the device. In lieu of form FD-2892, tapes for computer input or hard copy computer output may by submitted if equivalent in all elements of information as specified in form FD-2892. All formats proposed for use in lieu of form FD-2892 require initial review and approval by the Food and Drug Administration.

(c) The listing obligations of the initial distributor within the United States of an imported device are satisfied as follows:

(1) For those imported devices for which the initial distributor has also initiated or developed the specifications, form FD-2892 shall be submitted and the historical file maintained by the initial distributor.

(2) For those imported devices for which the initial distributor repackages or relabels the device, form FD-2892 shall be submitted and the historical file maintained by the initial distributor.

(3) The initial distributor is not required to submit a form FD-2892 for those imported devices for which such distributor did not initiate or develop the specifications for the device or repackage or relabel the device. However, the initial distributor shall submit, for each device, the name and address of the foreign manufacturer. Initial distributors shall also be prepared to submit, when requested by the Food and Drug Administration, the proprietary name, if any, and the common or usual name of each device for which they are the initial distributors.

(4) The initial distributor shall update the information required by paragraphs (c) (1), (2), and (3) of this section at the intervals specified in § 807.30.

e. In § 807.25, by revising the section heading and by adding new paragraph (f), to read as follows:

§ 807.25 Information required or requested for establishment registration and device listing.

* * * * *

(f) Form FD-2892 is the approved form for providing the device listing information required by the act. This required information includes the following:

(1) The identification by classification name and number, proprietary name, and common or usual name of each device being manufactured, prepared, propagated, compounded, or processed for commercial distribution that has not been included in any list of devices previously submitted on form FD-2892.

(2) The Code of Federal Regulations citation for any applicable standard for the device under section 514 of the act or section 358 of the Public Health Service Act.

(3) The assigned Food and Drug Administration number of the approved application for each device listed that is subject to section 505, 507, or 515 of the act.

(4) The name, registration number, and establishment type of every domestic or foreign device establishment under joint ownership and control of the owner or operator at which the device is manufactured, repackaged, or relabeled.

(5) Whether the device, as labeled, is intended for distribution to and use by the general public.

(6) Other general information requested on form FD-2892, i.e., (i) if the submission refers to a previously listed device, as in the case of an update, the document number from the initial listing document for the device, (ii) the reason for submission, (iii) the date on which the reason for submission occurred, (iv) the date that the form FD-2892 was completed, (v) the owner's or operator's name and identification number.

(7) Labeling or other descriptive information (e.g., specification sheets or catalogs) adequate to describe the intended use of a device when the owner or operator is unable to find on the Food and Drug Administration list in the device listing package, an appropriate classification name for the device.

f. By adding new § 807.30 to read as follows:

§ 807.30 Updating device listing information.

(a) Form FD-2892 shall be used to update device listing information. The preprinted original document number of each form FD-2892 on which the device was initially listed shall appear in block 2 on the form subsequently used to update the listing information for the device and on any correspondence related to the device.

(b) An owner or operator shall update the device listing information during each June and December or, at its discretion, at the time the change occurs. Conditions that require updating and information to be submitted for each of these updates are as follows:

(1) If an owner or operator introduces into commercial distribution a device identified with a classification name not currently listed by the owner or operator, then the owner or operator must submit form FD-2892 containing all the information required by § 807.25(f).

(2) If an owner or operator discontinues commercial distribution of all devices in the same device class, i.e., with the same classification name, the owner or operator must submit form FD-2892 containing the original document number of the form FD-2892 on which the device class was initially listed, the reason for submission, the date of discontinuance, the owner or operator's name and identification number, the classification name and number, the proprietary name, and the common or usual name of the discontinued device.

(3) If commercial distribution of a discontinued device identified on a form FD-2892 filed under paragraph (b)(2) of this section is resumed, the owner or operator must submit on form FD-2892 a notice of resumption containing: the original document number of the form initially used to list that device class, the reason for submission, date of resumption, and all other information required by § 807.25(f).

(4) If one or more classification names for a previously listed device with multiple classification names has been added or deleted, the owner or operator must supply the original document number from the form FD-2892 on which the device was initially listed and a supplemental sheet identifying the names of any new or deleted classification names.

(5) Other changes to information on form FD-2892 will be updated as follows:

(i) Whenever a change occurs only in the owner or operator name (block 6) or number (block 7), e.g., whenever one company's device line is purchased by another owner or operator, it will not be necessary to supply a separate form FD-2892 for each device. In such cases, the new owner or operator must follow the procedures in § 807.26 and submit a letter informing the Food and Drug Administration of the original document number from form FD-2892 on which each device was initially listed for those devices affected by the change in ownership.

(ii) The owner or operator must also submit update information whenever changes occur to the responses to the questions in blocks 12, 12a, 13, 13a, and 14 on form FD-2892, or whenever establishment registration numbers, establishment names, and/or activities are added to or deleted from blocks 15, 16, and 17 of form FD-2892. The owner or operator must supply the original document number from the form FD-2892 on which the device was initially listed, the reason for submission, and all other information required by § 807.25(f).

(6) Updating is not required if the above information has not changed since the previously submitted list. Also, updating is not required if changes occur in proprietary names, in common or usual names (blocks 10 and 11 of form FD-2892), or to supplemental lists of unclassified components or accessories.

g. By adding new § 807.31 to read as follows:

§ 807.31 Additional listing information.

(a) Each owner or operator shall maintain a historical file containing the labeling and advertisements in use on the date of initial listing, and in use after October 10, 1978, but before the date of initial listing, as follows:

(1) For each device subject to section 514 or 515 of the act that is not a restricted device, a copy of all labeling for the device;

(2) For each restricted device, a copy of all labeling and advertisements for the device;

(3) For each device that is neither restricted nor subject to section 514 or 515 of the act, a copy of all labels, package inserts, and a representative sampling of any other labeling.

(b) In addition to the requirements set forth in paragraph (a) of this section, each owner or operator shall maintain in the historical file any labeling or advertisements in which a material change has been made anytime after initial listing.

(c) Each owner or operator may discard labeling and advertisements from the historical file as follows:

(1) Five years after the date of the last shipment of a discontinued device by an owner or operator,

(i) All labeling that was not in use at the time of the last shipment of the device may be discarded, and,

(ii) All advertisements may be discarded, except for a representative sampling of all advertisements in use during the 12 months immediately preceding the last shipment of a restricted device.

(2) All labeling that was in use at the time of the last shipment of a discontinued device and a representative sampling of all advertisements in use during the 12 months immediately preceding the last shipment of a restricted device may be discarded 5 years after the date of the last shipment of the device or at the end of the anticipated useful life of the device.

(d) Location of the file:

(1) Currently existing systems for maintenance of labeling and advertising may be used for the purpose of maintaining the historical file as long as the information included in the systems fulfills the requirements of this section, but only if the labeling and advertisements are retrievable in a timely manner.

(2) The contents of the historical file may be physically located in more than one place in the establishment or in more than one establishment provided there exists joint ownership and control among all the establishments maintaining the historical file. If no joint ownership and control exists, the registered establishment must provide the Food and Drug Administration with a letter authorizing the establishment outside its control to maintain the historical file.

(e) Each owner or operator shall be prepared to submit to the Food and Drug Administration, only upon specific request, the following information:

(1) For a device subject to section 514 or 515 of the act that is not a restricted device, a copy of all labeling for the device.

(2) For a device that is a restricted device, a copy of all labeling for the device, a representative sampling of advertisements for the device, and for good cause, a copy of all advertisements for a particular device. A request for all advertisements will, where feasible, be accompanied by an explanation of the basis for such request.

(3) For a device that is neither a restricted device, nor subject to section 514 of 515 of the act, the label and package insert for the device and a representative sampling of any other labeling for the device.

(4) For a particular device, a statement of the basis upon which the registrant has determined that the device is not subject to section 514 or 515 of the act.

(5) For a particular device, a statement of the basis upon which the registrant has determined the device is not a restricted device.

(6) For a particular device, a statement of the basis for determining that the product is a device rather than a drug.

(7) For a device that the owner or operator has manufactured for distribution under a label other than its own, the names of all distributors for whom it has been manufactured.

h. In § 807.35, by revising paragraph (c) to read as follows:

§ 807.35 Notification of registrant.

* * * * *

(c) Although establishment registration and device listing are required to engage in the device activities described in § 807.20, validation of registration and the assignment of a device listing number in itself does not establish that the holder of the registration is legally qualified to deal in such devices and does not represent a determination by the Food and Drug Administration as to the status of any device.

i. By revising the section heading and text of § 807.37 to read as follows:

§ 807.37 Inspection of establishment registration and device listings.

(a) A copy of the forms FD-2891 and FD-2891a filed by the registrant will be available for inspection in accordance with section 510(f) of the act, at the Bureau of Medical Devices (HFK-124), Food and Drug Administration, Department of Health, Education, and Welfare, 8757 Georgia Avenue, Silver Spring, Md. 20910. In addition, there will be available for inspection at each of the Food and Drug Administration district offices the same information for firms within the geographical area of such district office. Upon request, verification of registration number or location of a registered establishment will be provided.

(b)(1) The following information filed under the device listing requirements will be available for public disclosure:

(i) Each form FD-2892 submitted;

(ii) All labels submitted;

(iii) All labeling submitted;

(iv) All advertisements submitted;

(v) All data or information that has already become a matter of public knowledge.

(2) Requests for device listing information identified in paragraph (b)(1) of this section should be directed to the Bureau of Medical Devices (HFK-124), Food and Drug Administration, Department of Health, Education, and Welfare, 8757 Georgia Avenue, Silver Spring, Md. 20910.

(3) Requests for device listing information not identified in paragraph (b)(1) of this section shall be submitted and handled in accordance with part 20 of this chapter.

j. In subpart C, by revising the section heading and text of § 807.40, to read as follows:

§ 807.40 Establishment registration and device listing for foreign manufacturers of devices.

(a) Foreign device establishments that export devices into the United States are requested to register in accordance with the procedures of sub-

part B of this part, unless exempt under subpart D of this part.

(b) Foreign device establishments that export devices into the United States, whether or not the establishment is registered, shall comply with the device listing requirements unless exempt from registration as stated in § 807.65. Those foreign owners or operators for which there exists joint ownership and control with a domestic establishment may have the domestic establishment submit listing information and maintain the historical file. A foreign owner or operator may authorize a domestic initial distributor to submit listing information when joint ownership and control does not exist, only if:

(1) The domestic distributor is the sole initial distributor for the foreign owner or operator's device; and

(2) The foreign owner or operator submits a letter to the Food and Drug Administration authorizing the initial distributor to list on its behalf and maintain the historical file.

(c) Except for a device imported or offered for import that has in effect an approved exemption for investigational use under section 520(g) of the act, a device may not be imported from a foreign device establishment into the United States unless it is listed at the interval specified for updating device listing information in § 807.30(b). The device listing information shall be in the English language.

(d) Foreign device establishments shall submit, as part of the device listing, the name and address of the establishment and the name of the individual responsible for submitting device listing information. Any changes in this information shall be reported to the Food and Drug Administration at the intervals specified for updating device listing information in § 807.30(b).

Effective date: This regulation shall be effective October 10, 1978.

(Secs. 301 (p) and (q)(2), 501, 502, 508, 510, 519, 701(a), 52 Stat. 1042-1043 as amended, 1049-1050 as amended, 1055, 76 Stat. 789, 794 as amended, 86 Stat. 562 as amended, 90 Stat. 564-580 (21 U.S.C. 331 (p) and (q)(2), 351, 352, 358, 360, 360f, 371(a)).)

Dated: August 16, 1978.

WILLIAM F. RANDOLPH,
Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 78-23757 Filed 8-24-78; 8:45 am]

[4110-03]

SUBCHAPTER E—ANIMAL DRUGS, FEEDS, AND RELATED PRODUCTS

PART 539—BULK ANTIBIOTIC DRUGS SUBJECT TO CERTIFICATION

PART 540—PENICILLIN ANTIBIOTIC DRUGS FOR ANIMAL USE

Sterile Amoxicillin Trihydrate; Sterile Amoxicillin Trihydrate for Suspension

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The regulations are amended to reflect approval of a new animal drug application (NADA) filed by Beecham Laboratories. The NADA provides for safe and effective use of sterile amoxicillin trihydrate for suspension for treating certain bacterial infections in dogs and cats. In addition, the regulations are amended to provide for certification of the bulk sterile amoxicillin trihydrate used in the manufacture of sterile amoxicillin trihydrate for suspension.

EFFECTIVE DATE: August 25, 1978.

FOR FURTHER INFORMATION CONTACT:

Robert A. Baldwin, Bureau of Veterinary Medicine (HFV-114), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, Md. 20857, 301-443-3420.

SUPPLEMENTARY INFORMATION: Beecham Laboratories, Division of Beecham, Inc., Bristol, Tenn. 37620, filed a NADA (55-091V) providing for use of sterile amoxicillin for suspension for treating dogs for certain bacterial infections of the respiratory tract, genitourinary tract, gastrointestinal tract, bacterial dermatitis, and soft tissues, and cats for certain infections of the upper respiratory tract, genitourinary tract, gastrointestinal tract, skin, and soft tissues. A companion application form 6, 62-015, provides for certification of the sterile amoxicillin trihydrate used in the manufacture of the drug.

In accordance with the freedom of information regulations and § 514.11(e)(2)(ii) of the animal drug regulations (21 CFR 514.11(e)(2)(ii)), a summary of the safety and effectiveness data and information submitted to support approval of this application is released publicly. The summary is available for public examination at the office of the Hearing Clerk (HFA-305), Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857, between 9 a.m. and 4 p.m., Monday through Friday.

Therefore, under the Federal Food, Drug, and Cosmetic Act (sec. 512 (i), (n), 82 Stat. 347, 350-351 (21 U.S.C. 360b (i), (n))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), parts 539 and 540 are amended as follows:

1. Part 539 is amended in subpart A by adding new § 539.3 to read as follows:

§ 539.3 Sterile amoxicillin trihydrate.

(a) *Requirements for certification—*(1) *Standards of identity, strength, quality, and purity.* Amoxicillin trihydrate is the trihydrate form of D(−) α-amino-*p*-hydroxybenzyl penicillin. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms and not nore than 1,050 micrograms of amoxicillin per milligram on an anhydrous basis.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) It passes the safety test.

(v) Its moisture content is not less than 11.5 percent and not more than 14.5 percent.

(vi) Its pH in an aqueous solution containing 2 milligrams per milliliter is not less than 3.5 and not more than 6.0.

(vii) Its amoxicillin content is not less than 90 percent on an anhydrous basis.

(viii) The acid-base titration concordance is such that the difference between the percent amoxicillin content when determined by nonaqueous acid titration and by nonaqueous base titration is not more than 6. The potency acid titration concordance is such that the difference between potency value divided by 10 and the percent amoxicillin content of the sample determined by the nonaqueous acid titration is not more than 6. The potency-base titration concordance is such that the difference between the potency value divided by 10 and the percent amoxicillin content of the sample determined by the nonaqueous base titration is not more than 6.

(ix) It is crystalline.

(x) It gives a positive identity test for amoxicillin trihydrate.

(2) *Labeling.* In addition to the labeling requirements prescribed by § 432.5(b) of this chapter, this drug shall be labeled "amoxicillin".

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 514.50 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, safety, moisture, pH, amoxicillin content, concordance, crystallinity, and identity.

(ii) Samples required:

(*a*) For all tests except sterility: 10 packages, each containing approximately 600 milligrams.